REMARKS

Applicants thank the Examiner for the courtesy of a personal interview on August 23, 2004. Applicants have cancelled claim 125, as discussed during the personal interview.

During the interview, the § 112 rejections from the most recent office action were generally discussed. Applicants will not reiterate the remarks regarding support for and written description of 60% identity to domains A and B, discussed during the personal interview. Applicants wish to emphasize the following points regarding the recitation of greater than 43% identity to the amino acid sequence set forth in SEQ ID NO:2, found in independent claims 58, 67, 76, 85-87 and 123.

Remarks regarding rejections under 35 U.S.C. § 112, first paragraph (written description)

The Examiner stated that the "specification does not disclose what amino acids of SEQ ID NO:2 can be altered such that the resultant amino acid sequences have at least 43% identity with SEQ ID NO:2, and 60% identity to domains A and B of SEQ ID NO:2, and retains their functional activity." Office Action of February 4, 2004 at page 6. As discussed during the personal interview and set forth below, Applicants respectfully submit that the combination of the disclosure of the specific chemical structure of the polypeptide sequence set forth in SEQ ID NO:2, coupled with the teachings in the specification concerning the characteristics of domains A and B and how to test for 22α-hydroxylase activity, provide adequate written description for the recitation of greater than 43% identity to SEQ ID NO:2.

The Federal Circuit addressed the written description requirement for DNA inventions in Enzo Biochem, Inc. v. Gen-Probe Inc., 296 F.3d 1316, 63 USPQ2d 1609 (Fed. Cir. 2002). The Enzo court adopted the standard that "the written description requirement can be met by 'showing that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics . . . i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics.'" Id. at 1324, 63 USPQ2d at 1613. The instant specification meets this standard.

Four characteristic domains of P450 proteins were disclosed by the inventors to be present in DWF4. Specification at page 53, lines 25-33. A detailed discussion of conserved and non-conserved amino acid positions in these domains was presented by the inventors. Specification at page 55, lines 10-27. The fact that DWF4 clustered with P450s found in a wide variety of organisms rather than those unique to plants was described by the inventors. Specification at page 55, line 28 to page 56, line 13. The anchor region and the proline-rich region of DWF4 were described by the inventors in Figures 2 and 3. A discussion of how to screen for 22α-hydroxylase activity was provided by the inventors. Specification, at page 68, line 12 to page 69, line 22. Variants with "one or more amino acid additions, substitutions (generally conservative in nature) and/or deletions, relative to the native molecule, so long as the modifications do not destroy the desired activity" were indicated by the inventors as included in the invention. Specification at page 25, lines 18-22.

Given the above, one of ordinary skill would have recognized from reading the specification that the structure and functional characteristics of SEQ ID NO:2 were disclosed, that structural and functional characteristics of four P450 domains were disclosed, and that structural and functional characteristics of the anchor and proline-rich regions were disclosed. One of ordinary skill would have recognized from these teachings, coupled with teachings on how to test for 22α-hydroxylase activity, that Applicants described and were in possession of a polypeptide having greater than 43% sequence identity to SEQ ID NO:2 as recited in independent claims 58, 67, 76, 85-87, and 123.

The Examiner also referred to an article by Nebert et al. (Nebert) published in 1991 concerning P450 nomenclature. Nebert et al., DNA and Cell Biology 10:1-14 (1991). The Examiner indicated that, according to Nebert, the P450 classification system is arbitrary. Office Action of February 4, 2004 at page 7. However, an update of the P450 nomenclature system was published in 1996. Nelson et al., Pharmacogenetics 6:1-42 (1996) ("Nelson"). According to the 1996 update, a "P450 protein sequence from one gene family usually is defined as having $\leq$40% amino acid identity to a P450 protein from any other family. This definition of a P450 gene family was originally an arbitrary decision, but unexpectedly has turned out to be very useful."

Nelson, page 4, left-hand column. In view of Nelson, it was known to one of ordinary skill as of the 1999 priority date of the instant application that this P450 classification system was useful. One of ordinary skill would not have considered a recitation of greater than 43% sequence identity to be arbitrary.

The Examiner also indicated that the 1996 Nelson article emphasized that "similarities in enzymatic activities *cannot* be used to classify genes within any gene family or subfamily." Office Action of 2-4-04 at page 7 (emphasis in original). The passage referred to by the Examiner in the 1996 Nelson article, however, states that similarities in enzymatic activity alone cannot be used to classify genes within any given family or subfamily. The passage adds that "[i]t is worth repeating that properties in addition to sequence may provide important information . . .." and goes on to mention various properties that may be helpful in nomenclature assignments. In other words, Nelson is emphasizing that a combination of structural and functional characteristics are generally useful in determining P450 nomenclature. Thus, Nelson supports the conclusion that one of ordinary skill in the art would have recognized from the combination of structural and functional characteristics disclosed in the instant specification that polypeptides having greater than 43% identity to SEQ ID NO:2 were described and invented by the present inventors.

The fact that SEQ ID NO: 2 variants having 22α-hydroxylase activity are not specifically listed in the instant specification or in a Sequence Listing is not necessarily dispositive of whether the specification satisfies the written description requirement. Applicants wish to bring to the Examiner's attention a recent non-binding decision of the Board of Patent Appeals and Interferences, in which a rejection for lack of written description was reversed by the Board. Ex parte Sun, Appeal No. 2003-1993 (Bd. Pat App. Int., 2004). A copy of Ex parte Sun is enclosed herewith. The patent specification at issue in Sun described the chemical structure of a particular polynucleotide encoding a particular polypeptide, described the chemical structure of the particular polypeptide, and provided an example of how to screen for functional activity of the particular polypeptide. The Sun specification did not present a species with 80% identity to the polypeptide and functional activity. Nevertheless, the Board did not find "the fact that the

specification does not specifically teach the structure of a species with 80% identity and [the claimed function] to be dispositive of the written description issue here." Sun at 8.

Applicants note that Sun is a non-precedential opinion, involving claims that are somewhat different from the claims pending in the instant application. However, it is Applicants' position that, similar to Sun, the instant specification provides sufficiently detailed, relevant identifying characteristics to show that the inventors recognized that they had invented what is now claimed. Such a conclusion is consistent with the standard adopted in Enzo Biochem, Inc. v. Gen-Probe Inc., 296 F.3d 1316, 63 USPQ2d 1609 (Fed. Cir. 2002).

Finally, polynucleotides or polypeptides of the invention can have various percentage ranges of sequence identity, including 43%-60%, 60%-70%, 70-85%, 85-90%, 90-95%, and 95-98% sequence identity, as described by the inventors in the instant specification. Specification, at page 18, lines 9-15 and page 42, lines 25-29. Based on the recitation of percentage sequence identities provided in the instant specification, one of ordinary skill would have also recognized that there is adequate written description for the recitation of even higher percentages of sequence identity to SEQ ID NO:2, as found in dependent claims 59-61, 68-70, 77-79, 95-96, 101-102, 107-108, 113-114, and 119-122.

Remarks regarding rejections under 35 U.S.C. § 112, first paragraph (enablement)

The Examiner asserted that the "specification does not disclose how to make the claimed polynucleotides that encode proteins that differ from SEQ ID NO:2 and which still retain its functional activity. The specification does not teach what amino acids one skilled in the art is to change to produce the claimed products." Office Action of February 4, 2004 at page 9. As discussed during the personal interview and in the remarks below, Applicants respectfully submit that the teachings in the specification concerning the characteristics of domains A, B and C, the heme-binding domain, the anchor and proline-rich regions, and how to test for 22α-hydroxylase activity, enable one of ordinary skill to make and use polynucleotides encoding polypeptides having greater than 43% identity to SEQ ID NO:2.

The instant specification provides detailed guidance as to conserved amino acid residues within the domains and the anchor and proline-rich regions of a 22α-hydroxylase. Specification, at page 55, lines 10-27; Figure 2; and Figure 3. The specification provides detailed guidance on how to measure 22α-hydroxylase activity. Specification, at page 68, line 12 to page 69, line 22. Applicants submit that it is a routine matter to convert from an amino acid sequence to the nucleotide sequence that encodes that polypeptide. Thus, no more than routine experimentation would have been needed to make polynucleotides encoding polypeptides having greater than 43% identity to SEQ ID NO: 2. The specification provides extensive guidance on how to perform plant transformation. Specification at page 37, line 29 to page 39, line 14. Thus, no more than routine experimentation would have been required to make transgenic plants containing such polynucleotides.

CONCLUSION

In view of the above, Applicants submit that the instant specification provides adequate written description and enablement for the recitation of greater than 43% identity to the amino acid sequence set forth in SEQ ID NO:2, found in independent claims 58, 67, 76, 85-87 and 123. Applicants respectfully request reconsideration and allowance of all pending claims.

No fee is believed to be due. Please apply any charges or credits to deposit account 06-1050.

Respectfully submitted,

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Ronald C. Lundquist, Ph.D.
Reg. No. 37,875

Fish & Richardson P.C., P.A.
60 South Sixth Street
Suite 3300
Minneapolis, MN 55402
Telephone: (612) 335-5070
Facsimile: (612) 288-9696

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